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C07K 14/00	A2	(43) International Publication Date: 4 May 2000 (04.05.00)		
(21) International Application Number: PCT/0 (22) International Filing Date: 28 October 1999	US99/254 9 (28.10.9	(71) Applicant (for all designated States except US): INCYTE PHARMACEUTICALS, INC. [US/US]; 3174 Porter Drive, Palo Alto, CA 94304 (US).		
(30) Priority Data: 09/181,711 28 October 1998 (28.10.9 Not furnished 28 October 1998 (28.10.9 09/209,547 11 December 1998 (11.12 Not furnished 11 December 1998 (11.12 09/313,457 17 May 1999 (17.05.99) Not furnished 17 May 1999 (17.05.99) (63) Related by Continuation (CON) or Continuation (CIP) to Earlier Applications	98) [2.98) [2.98) [1 [(72) Inventors; and (75) Inventors/Applicants (for US only): TANG, Y., Tom [CN/US]; 4230 Ranwick Court, San Jose, CA 95118 (US). YUE, Henry [US/US]; 826 Lois Avenue, Sunnyvale, CA 94087 (US). HILLMAN, Jennifer, L. [US/US]; 230 Monroe Drive #12, Mountain View, CA 94040 (US). CORLEY, Neil, C. [US/US]; 1240 Dale Avenue #30, Mountain View, CA 94040 (US). GUEGLER, Karl, J. [CH/US]; 1048 Oakland Avenue, Menlo Park, CA 94025 (US). BAUGHN, Mariah, R. [US/US]; 14244 Santiago Road, San Leandro, CA 94577 (US). AU-YOUNG, Janice [US/US]; 1419 Kains Avenue, Berkeley, CA 94702 (US).		
US 09/20 Filed on 11 December 1998 US 09/31 Filed on 17 May 1999	3,457 (CI	8) (74) Agents: BILLINGS, Lucy, J. et al.; Incyte Pharmaceuticals, Inc., 3174 Porter Drive, Palo Alto, CA 94304 (US).		

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Published

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(54) Title: GROWTH FACTOR RELATED MOLECULES

1 1	MRGTI	RLA	LLAL	VLA- VAAW	A C S M G C	GELAPAI GEAI	R C Y V K C Y T	2777282 GI 1536902
28 28	C P E P	TGV MTS	SDCV ASCR	TIAT	CKPE	ETMCKTT DTACMTT	LYSR	2777282 GI 1536902
58 58	EIVY	PFO	G D S T Q S P V	VTKS VTRS	CASK CSSS	CKPSDVI CVATDPI	GIGO SIGA	2777282 GI 1536902
88 88	TLPV	s c c	NTEL FRDL	CNVD CNSE	GAPA	LNSLHC	ALTL	2777282 GI 1536902
118 103	LPLL:	SLR	L L	·				2777282 GI 1536902

(57) Abstract

The invention provides human growth factor related molecules (GFRP) and polynucleotides which identify and encode GFRP. The invention also provides expression vectors, host cells, antibodies, agonists, and antagonists. The invention also provides methods for diagnosing, treating, or preventing disorders associated with expression of GFRP.

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English

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(63) Related by continuation (CON) or continuation-in-part (CIP) to earlier applications:

US 09/209,547 (CIP) Filed on 11 December 1998 (11.12.1998) 09/313,457 (CIP) US Filed on 17 May 1999 (17.05.1999) US 09/181,711 (CIP) Filed on 28 October 1998 (28.10.1998) US Not furnished (CIP) Filed on 28 October 1998 (28.10.1998) US Not furnished (CIP) Filed on 11 December 1998 (11.12.1998) (72) Inventors; and (75) Inventors/Applicants (for US only): TANG, Y., Tom [CN/US]; 4230 Ranwick Court, San Jose, CA 95118 (US). YUE, Henry [US/US]; 826 Lois Avenue, Sunnyvale, CA 94087 (US). HILLMAN, Jennifer, L. [US/US]; 230 Monroe Drive #12, Mountain View, CA 94040 (US). CORLEY, Neil, C. [US/US]; 1240 Dale Avenue #30, Mountain View, CA 94040 (US). GUEGLER, Karl, J. [CH/US]; 1048 Oakland Avenue, Menlo Park, CA 94025 (US). BAUGHN, Mariah, R. [US/US]; 14244 Santiago Road, San Leandro, CA 94577 (US). AU-YOUNG, Janice [US/US]; 1419 Kains Avenue, Berkeley, CA 94702 (US).

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Drive, Palo Alto, CA 94304 (US).

- (74) Agents: BILLINGS, Lucy, J. et al.; Incyte Pharmaceuticals, Inc., 3174 Porter Drive, Palo Alto, CA 94304 (US).
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[Continued on next page]

(54) Title: GROWTH FACTOR RELATED MOLECULES

MRGTRLALLALVLA - - - ACGELAPALRCYV 2777282 1 MASRWAVQLLLVAAWSMGCGE---ALKCYT GI 1536902 1

28 CPEPTGVSDCVTIATCTTNETMCKTTLYSR 2777282 28 CKEPMTSASCRTITRCKPEDTACMTTLVTV GI 1536902

EIVYPFOGDSTVTKSCASKCKPSDVDGIGO 2777282 58

encode GFRP. The invention also provides expression vectors, host cells, antibodies, agonists, and antagonists. The invention also provides methods for diagnosing, treating, or preventing disorders associated with expression of GFRP.





(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

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INTERNATIONAL SEARCH REPORT

International Application No PCT/US 99/25458

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N15/12 C12N5/10 C12N15/63 C07K14/475 C07K16/22 A61K38/18 According to International Patent Classification (IPC) or to both national classification and IPC B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) IPC 7 C07K A61K Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) C. DOCUMENTS CONSIDERED TO BE RELEVANT Category ° Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No. P,X WO 99 46281 A (GENENTECH, INC.) 1-16,19 16 September 1999 (1999-09-16) page 41, line 25 -page 42, line 4 page 157, line 20 - line 30; figures 184,185; example 74 X MARRA, M. ET AL.: "The WashU-HHMI mouse 1-6,9-13 EST project" EMBL DATABASE, EMEST36.MMAA59621; ACCESSION-NO.: AA259621, 19 March 1997 (1997-03-19), XP002140754 Υ the whole document 7,8, 14-16 -/--Further documents are listed in the continuation of box C. Х Patent family members are listed in annex. Special categories of cited documents : T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the *A* document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to filing date document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention citation or other special reason (as specified) cannot be considered to involve an inventive step when the document is combined with one or more other such docu-"O" document referring to an oral disclosure, use, exhibition or other means ments, such combination being obvious to a person skilled document published prior to the international filing date but later than the priority date claimed in the art "&" document member of the same patent family Date of the actual completion of the international search Date of mailing of the international search report 21 June 2000 14. 09.00 Name and mailing address of the ISA Authorized officer European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Donath, C

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10		PCT/US 99/25458
	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	
ategory °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SOARES, M.B.: "Program for rat gene discovery and mapping" EMBL DATABASE, EMEST6.AI112088; ACCESSION-NO.: AI112088, 4 September 1998 (1998-09-04), XP002140755	1-6,9-13
Υ .	the whole document	7,8, 14-16
A	RIDGE, R.J. AND SLOANE, N.H.: "Partial N-terminal amino acid sequence of the anti-neoplastic urinary protein (ANUP) and the anti-tumour effect of the N-terminal nonapeptide of the unique cytokine present in human granulocytes" CYTOKINE, vol. 8, no. 1, January 1996 (1996-01), pages 1-5, XP000915567 cited in the application the whole document	1,2,15, 16,19
A	BRANDT R. ET AL.: "Identification and biological characterization of an epidermal growth factor-related protein: Cripto-1" THE JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 269, no. 25, 24 June 1994 (1994-06-24), pages 17320-17328, XP000910201 the whole document	

INTERNATIONAL SEARCH REPORT

International application No. PCT/US 99/25458

Box I Ob	servations where certain claims wer found uns archable (Continuation fitem 1 of first sheet)
This Internal	tional Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
	aims Nos.: cause they relate to subject matter not required to be searched by this Authority, namely:
bo	lthough claim 19 is directed to a method of treatment of the human/animal ody, the search has been carried out and based on the alleged effects of the ompound/composition.
bed	tims Nos.: 17,18,20 cause they relate to parts of the International Application that do not comply with the prescribed requirements to such extent that no meaningful International Search can be carried out, specifically:
1	ee FURTHER INFORMATION sheet PCT/ISA/210
	uims Nos.: cause they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II Ob	servations where unity of invention is lacking (Continuation of item 2 of first sheet)
This Internat	ional Searching Authority found multiple inventions in this international application, as follows:
See	e additional sheet
1. As sea	all required additional search fees were timely paid by the applicant, this International Search Report covers all urchable claims.
2. As of a	all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment ony additional fee.
3. As cov	only some of the required additional search fees were timely paid by the applicant, this International Search Report ers only those claims for which fees were paid, specifically claims Nos.:
resi	required additional search fees were timely paid by the applicant. Consequently, this International Search Report is tricted to the invention first mentioned in the claims; it is covered by claims Nos.: - 20 (partially)
Remark on f	Protest The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

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Claims Nos.: 17,18,20

Claims 17 and 18 concern an agonist and an antagonist of GFRP-1, respectively. Claim 20 concerns a method which makes use of the antagonist of GFRP-1. The agonist or the antagonist of GFRP-1. The agonist and antagonist are only defined by the method which can be used in order to identify these compounds. Since it is completely unclear which kind of substances will be identified by the respective method and since in the specification no concrete examples for these kind of substances are given, the scope of said claims is totally ambiguous and undefined. Moreover, it cannot be excluded that even substances known in the art may be recognized as agonists or antagonists of GFRP-1.

In view of the wording of the claims presently on file, which render it difficult, if not impossible, to determine the matter for which protecztion is sought, the present International application fails to comply with the clarity requirements of Article 6 PCT to such an extent that a meaningful search of the claims is impossible. Consequently, the search has been carried out for those parts of the application which do appear to be clear, namely claims 1-16 and 19 (all partially).

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Claims: 1-20 (partially)

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Claims 1-20 (partially) refer to a purified human growth factor related molecule (GFRP-1) comprising the amino acid sequence as shown in SEQ ID NO:1 and the polynucleotide encoding said GFRP-1. GFRP-1 is 125 amino acids in length and has chemical and structural similarity with ANUP and with mouse ARS component B precursor. Furthermore, the claims concern expression vectors, host cells, antibodies, agonists, antagonists, and methods for diagnosing, treating or preventing disorders associated with expression of GFRP-1.

2. Claims: 1-20 (partially)

Claims 1-20 (partially) refer to a purified human growth factor related molecule (GFRP-2) comprising the amino acid sequence as shown in SEQ ID NO:2 and the polynucleotide encoding said GFRP-2. GFRP-2 is 127 amino acids in length and has chemical and structural similarity with hTECK, with human Dvic-1 C-C chemokine, and with mouse CC chemokine ALP. Furthermore, the claims concern expression vectors, host cells, antibodies, agonists, antagonists, and methods for diagnosing, treating or preventing disorders associated with expression of GFRP-2.

3. Claims: 1-20 (partially)

Claims 1-20 (partially) refer to a purified human growth factor related molecule (GFRP-3) comprising the amino acid sequence as shown in SEQ ID NO:3 and the polynucleotide encoding said GFRP-3. GFRP-3 is 147 amino acids in length and has chemical and structural similarity with chicken follistatin and with human follistatin-related protein FLRG. Furthermore, the claims concern expression vectors, host cells, antibodies, agonists, antagonists, and methods for diagnosing, treating or preventing disorders associated with expression of GFRP-3.

4. Claims: 1-20 (partially)

Claims 1-20 (partially) refer to a purified human growth factor related molecule (GFRP-4) comprising the amino acid sequence as shown in SEQ ID NO:4 and the polynucleotide encoding said GFRP-4. GFRP-4 is 345 amino acids in length and has chemical and structural similarity with human BMP-1 and with chicken BMP-1. Furthermore, the claims concern expression vectors, host cells, antibodies, agonists, antagonists, and methods for diagnosing, treating or preventing disorders associated with expression of GFRP-4.



information on patent family members

International Application No PCI/US 99/25458

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9946281 A	16-09-1999	AU 3072199 A AU 3075099 A WO 9947677 A AU 1532499 A EP 1032667 A WO 9927098 A AU 3757099 A WO 9954467 A AU 1070399 A EP 1025227 A WO 9920756 A	27-09-1999 11-10-1999 23-09-1999 15-06-1999 06-09-2000 03-06-1999 08-11-1999 28-10-1999 10-05-1999 09-08-2000 29-04-1999
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